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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,752	01/27/2004	Darrell H. Carney	3033.1008-008	2963

21005 7590 04/20/2005

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EXAMINER	
MONDESI, ROBERT B	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,752	CARNEY, DARRELL H.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26,28 and 34-42* is/are pending in the application.

4a) Of the above claim(s) *7,10-13,16-25,34,36,38 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to restriction requirement

Applicants' election with traverse of election of SEQ ID No. 5, and the further election of moieties, R1= H and R2=NH_2, claims **1-16, 26, 28 and 35-42** in amendment, filed January 24, 2005 is acknowledged. The traversal is on the ground(s) that the examiner has not set forth any groups of claims to independent or distinct inventions; furthermore the examiner has presented a peptide analysis of the claims in terms of "peptide compounds" which has been assumed to be patentably distinct because each one "is capable of eliciting a specific immune response and can be used to produce an antibody". Applicants state further that they do not understand what reasoning connects the fact that the different peptides can produce different immune responses, with the conclusion that the claims to methods using peptides identified with different SEQ ID Nos represents distinct or different inventions. Applicants also state that the examiner has mentioned "Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and search restriction for examination purposes has been indicated as proper; however the examiner has not reported a different classification for different groups of the claims. The applicants also state that to formulate a search strategy, it should be noted that the peptides designated aa SEQ ID Nos 2-8 have similar structures, so not all need to be searched individually.

The applicants' assertions have been found persuasive but only in part. The examiner agrees that since the claims are drawn to a method of use, the reasoning with regards to the different compounds of the invention eliciting a different immune response is not appropriate and that the distinction of the methods of the invention based on classification is not appropriate. However the examiner does not agree that the peptides designated as SEQ ID NOs 2-8 have the same structure and would not have to be searched individually. The peptide designated as SEQ ID NO: 2 is a peptide with 23 residues, the peptide designated as SEQ ID NO: 3 is a peptide with 33 residues, the peptide designated as SEQ ID No: 7 is a peptide with 4 residues, and the peptide designated as SEQ ID No: 8 is a peptide with 13 residues. A person of ordinary skill in the art would not agree with the fact that a peptide with 4 amino acids has the same primary amino acid structure as a peptide with 33 amino acids. Also as far as searching the appropriate amino acid data bases is concerned, due to the difference in the primary amino acid structure , a search for SEQ ID NO: 4 can not be performed simultaneously as a search for SEQ ID NO: 7; and two independent data base searches are required, one for SEQ ID NO: 7 and another for SEQ ID NO: 4.

Therefore the requirement is still deemed proper and is made FINAL. **Claims 27, 29-33** have been cancelled. **Claims 35-42** are new. **Claims 1-26, 28 and 34-42** are pending in this application. **Claims 7, 10-13, 16-25, 34, 36 and 38-39** are withdrawn. **Claims 1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41** are currently under examination.

Priority

The current application filed on January 27, 2004 is CON of PCT/US02/01151 filed on January 16, 2002, which in turn claims priority to provisional application 60/308,198 filed on July 27, 2001.

Preliminary Amendment

The preliminary amendment filed June 03, 2004 has been entered.

Information Disclosure Statement

The IDS(s) filed January 27, 2004, June 03, 2004 and March 02, 2005 have been received and is signed and considered, a copy of the PTO 1449 is attached to the following document.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 8 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In **claims 5, 8 and 14** the applicants cite thrombin peptide derivatives wherein the thrombin peptide derivatives differ by one, two or three amino acids at positions 1-9 and 14-23 in the amino acid sequence of the thrombin peptide derivatives comprising the amino acid sequence designated as SEQ ID NO: 5. The applicants also cite truncated N-terminal and C-terminal thrombin peptide fragments of the thrombin peptide derivatives that are at least 14 amino acids and 18 amino acids long respectively. However the applicants have failed to provide a written description of the substitutions and deletions that would provide adequate support of the claimed invention. The applicants have not stated where (the exact position of the a.a. residue) in the stated amino acid sequence the substitution or deletion is to occur, or in the case of substitutions, the actual substituted amino acid. Presently the alterations are presented in a format that provides a various number of alternatives.

Furthermore the claims are drawn to a genus of polypeptides that is defined by an unclear functional relationship to the thrombin peptide derivative comprising the amino acid sequence of SEQ ID No: 5. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is that the thrombin peptide derivatives have been

subjected to undetermined substitutions and deletions. The specification does not identify any particular substitutions or deletions that must be characteristic of the claimed genus. The only adequately described species is the thrombin peptide derivative comprising the amino acid sequence of SEQ ID No: 5. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the a14 that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not it clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116), As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF' s were found to be unpatentable due to lack of written description for that broad class. The specification provided only

the bovine sequence. Therefore, only the thrombin peptide derivative comprising the amino acid sequence of SEQ ID No: 5, but not the full breadth of the claim meets the written description provision of 35 U. S.C. 112, first paragraph. Applicant is reminded that *Vas-cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision.

Claims 1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41 cite a method of promoting healing of a chronic skin ulcer on a subject comprising the step of contacting skin ulcer with an effective amount of an agonist; however the applicants have not stated the nature or the end result of the response initiated by the agonist. An agonist binds a receptor and initiates a change in the function of the cell; presently the applicants have not explained the change that is caused by the agonist.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Carney et al. U.S. Patent No. 5,352,664.

The examiner has provided an accompanying reference that defines venous stasis ulcer, diabetic ulcers and pressure ulcers as examples of chronic wounds (page 2, lines 1-3; HGS Backgrounder, September 2000).

Carney et al. teach that their invention provides a number of thrombin derivatives and methods useful for stimulating cell proliferation and promoting wound healing as well as methods useful in inhibiting wound healing, scar tissue formation, formation of tissue adhesions, and tumor metastasis and angiogenesis. The invention is based on the discovery that one may formulate polypeptide thrombin derivatives, or their physiologically functional equivalents, which selectively inhibit the interaction of thrombin with its high-affinity receptor or which mimic the stimulatory effects of thrombin (column 3, lines 20-30).

Carney et .al teach further that accordingly, the invention, in its most general and overall scope, relates to synthetic or naturally derived polypeptide agonists and antagonists of thrombin receptor mediated events. Both of these classes of agents possess a thrombin receptor binding domain which includes a segment of the polypeptide that is capable of selectively binding to the high-affinity thrombin receptor (column 3, lines 31-37).

Carney et al. disclose that in one embodiment of the invention provides for a polypeptide containing specific amino acid sequences such as polypeptide compound in which the thrombin receptor domain includes the amino acid sequence Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-

Asp-Ser-Gly-Gly-Pro-Phe-Val (column 4, lines 29-32). The mentioned amino acid sequence is identical to the amino acid sequence of the elected peptide of the present application designated as SEQ ID No: 5.

Carney et al. also teach The invention also provides for a pharmaceutical composition for promoting wound healing which includes of a therapeutically effective concentration of any of the compounds described above combined with a pharmaceutically acceptable excipient and typically, such compositions include, for example, sufficient concentrations of the polypeptides to effect a stimulatory action on the thrombin receptor as demonstrated herein (column 4, lines 32-40).

Carney et al. teach In addition, methods are provided which employ thrombin agonists to promote wound healing. One such method includes applying to the wound a therapeutically effective amount of a polypeptide derivative of thrombin, or a physiologically functional equivalent thereof, which has a thrombin receptor-binding domain. In general, thrombin is applied in amount sufficient to achieve fibroblast stimulation and thereby stimulate tissue regeneration. In that such methods typically involve topical application to a wound possible sytstemic toxicity is not believed to be a problem (column 5, lines 1-7).

Thus Carney et al. teach all the elements of **Claims 1-6, 8-9, 14-15, 26, 28, 35, 37 and 40-41** and these claims are anticipated under 35 USC 102(b).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B. Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi
04-05-05

JON WEBER
SUPERVISORY PATENT EXAMINER